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Fragmentation of methylmethacrylate: A cause of late failure of total hip replacement

A case report

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Summary. Extensive localized bone lysis in the femur following implantation of a metal-on-metal total hip prosthesis was observed. Fragmentation of the cement occurred 10 years after implantation. Histologic and ultrastructural features of macrophages are consistent with the hypothesis that particles from the acrylic resin were the factors stimulating the macrophagic reaction. Both mechanical factors and changes of the physico-chemical properties of the cement may have an etiologic role.

A foreign-body reaction to particles released from the total hip replacement is a common cause of implant failure. Histologically, polyethylene and metallic debris are easily identified, but no direct evidence of methylmethacrylate in the tissues is possible. Fragmentation of the acrylic cement produced, in this case, an extensive, localized bone lysis in the femur and allowed a study of the tissue response to this type of material debris.

Case report

A 70-year-old man had a right total hip replacement in 1975 for severe osteoarthritis. There was no history of infection or trauma; osteoarthritis was present in the controlateral hip. A metal-on-metal McKee-Farrar prosthesis was inserted and fixed with Simplex P bone cement which did not contain barium sulphate. The postoperative course was uncomplicated and the patient regained excellent function of his hip. Five years later, total hip replacement was carried out on the left side.

The patient was satisfied with the results of the operation until September 1985, when he started to complain of pain in his right thigh. Roentgenograms taken in May 1986 showed osteolysis of the cortical bone at the level of the tip of the stem. The bone had been normal in control radiograms 1 year earlier (Fig. 1a, b). The patient refused revision or other surgical diagnostic procedures. ESR, leukocyte count, serum proteins, electrophoretic pattern, acid and alkaline phosphatase, and chest radiograms were normal. There was no other evidence of infection or neoplasm. The patient was advised to walk with a cane.

On July 1986 he was admitted for a fracture of the femur localized in correspondence to the osteolitic process (Fig. 1c). Laboratory tests were normal with no evidence of infection. Revision was performed through an anterolateral approach. Both the cup and the stem were not loosened and it was necessary to open a win-

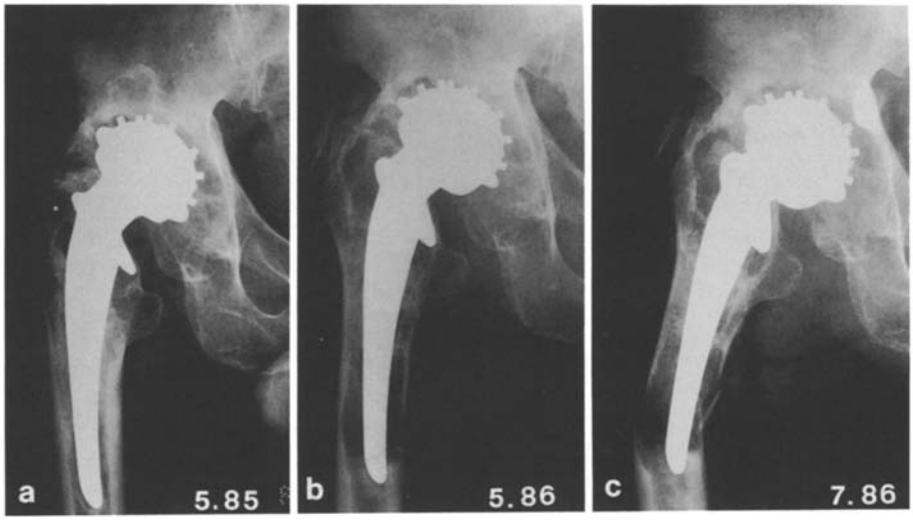
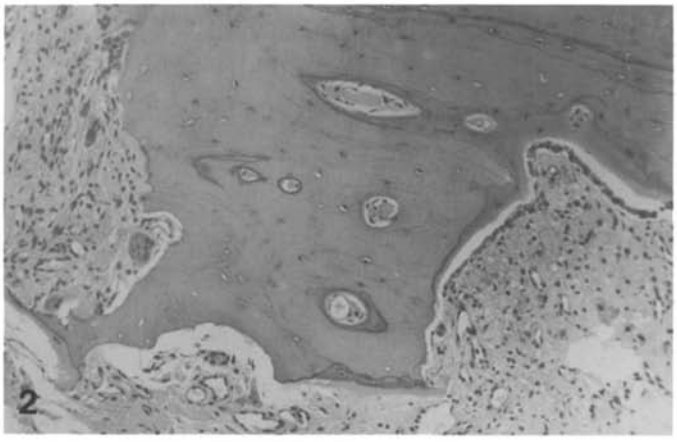
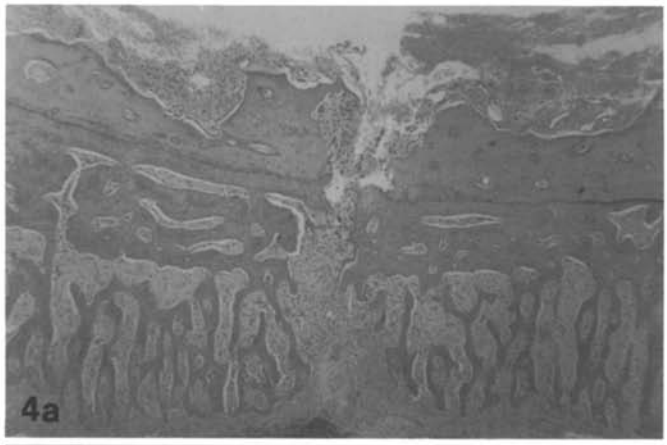
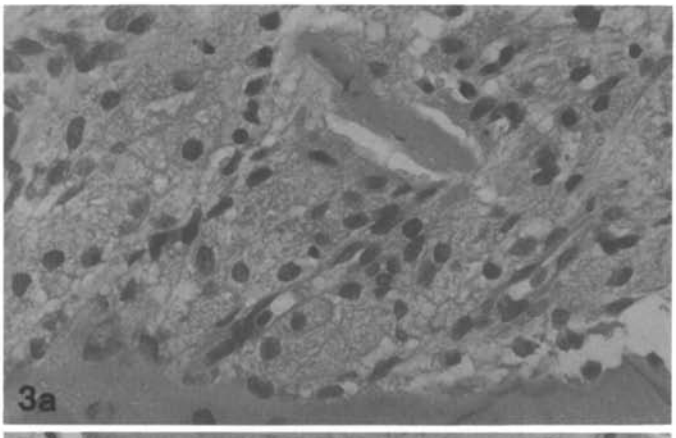
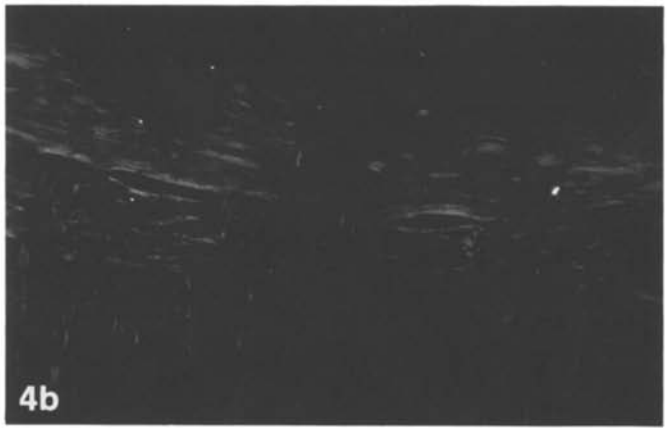


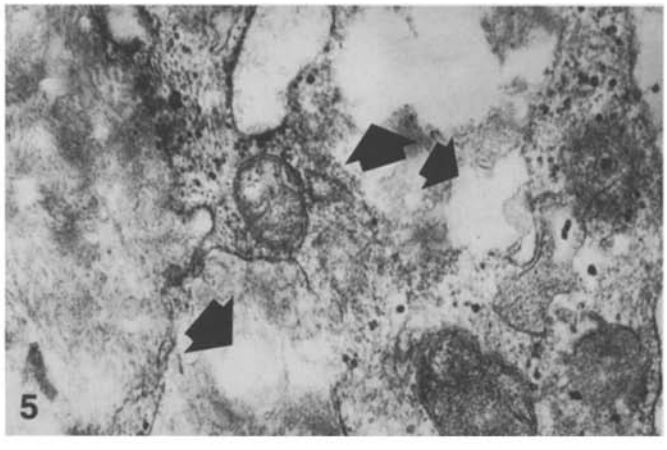
Fig. 1. a No lysis was present in the femur 10 years after prosthesis implantation. **b** Extensive, localized bone resorption developed from the 10th to the 11th year, leading to femoral fracture 2 months later (**c**)











dow in the anterior cortex to remove the stem and the cement from the proximal fragment of the femur. The osteolytic area at the site of the fracture was filled with a grayish-yellow, firm tissue which was curetted and examined histologically. Cultures of the material were negative. The distal cement of the stem was very brittle, and pulverized when it was touched. However, the cement of the cup and that of the proximal stem was of normal consistency.

A long-stem Charnley prosthesis was inserted and the defect in the femur filled with acrylic cement; the window in the anterior cortex was tightened with Partridge plastic bands. After the operation, weight bearing was restrained, but after 2 months a dislocation of the head of the prosthesis was observed. In February 1987, revision was carried out and a new stem inserted. After 3 months, walking with a cast was allowed.

Specimens from the osteolytic area were fixed with neutral formalin (10%), routinely processed, and stained with hematoxylin-eosin. Cortical bone was decalcified in EDTA before embedding. X-ray energy-dispersive analysis was performed on routine sections after removal of the coverslip and observation with the scanning electron microscope. Specimens for transmission electron microscopy were fixed in 4% glutaraldehyde, postfixed in 1% osmium tetroxide, and embedded in Epon. Sections were stained with uranyl acetate and lead citrate.

Pathological findings

Most of the soft tissue curetted from the osteolysis consisted of a sheet of macrophages with a clear granular cytoplasm; fibrin and hemorragic and necrotic material were also present. Foreign-body giant cells were associ-

Fig. 2. Irregular contour of the endosteal surface: osteoclasts are present, but most of the old resorption lacunae are occupied by macrophages or by active osteoblasts (*right side* of the figure). HE, × 86

Fig. 3. a Macrophages lining the bone surface; the cells have a clear and granular cytoplasm, but no particles were identified by polarized-light examination or by analytical methods. **b** Bone is invaded by macrophages through vascular canals; these cells are observed either in the vessel lumen (*empty arrow*) or between the bone and the endothelial wall (*full arrows*). HE, × 340

Fig. 4a, b. Section of the cortex at the level of the osteolysis: bright field (**a**) and polarized light (**b**). The endosteal surface of the cortex has undergone extensive resorption and presents a "moth-eaten" aspect. Two layers of periosteal apposition are evident: the inner represents a reaction to endosteal resorption (the bone is denser and remodeling more advanced); the outer is periosteal callus of the fracture. HE, × 21

Fig. 5. Large, secondary lysosomes are present in the cytoplasm of macrophages. The negative image of the material contained inside the lysosome appears as a globular, electron-transparent area (*arrows*). TEM, × 80000

ated with globular, empty spaces from 100 μm to 1 mm in diameter. No opaque particles nor birefringent material were observed in any of the sections. Neither metals nor barium were detected by X-ray energy-dispersive analysis. There were no inflammatory cells. The cortex of the femur was very thin, with an irregular inner surface and many resorption lacunae. Osteoclasts were numerous but osteoblastic activity was also present (Fig. 2). The sheet of macrophages filled inactive resorption lacunae and penetrated into all the cavities present on the inner surface of the cortical bone (Fig. 3 a). Invasion of the haversian canals was a constant finding, and macrophages were observed both inside vessels and outside the endothelial wall, in direct contact with the bone (Fig. 3b). Periosteal apposition was very active and the outer cortex was formed by a layer of trabeculae oriented perpendicular to the circumference of the diaphysis (Fig. 4). Ultrastructurally, the cytoplasm of the macrophages presented large, secondary lysosomes which contained an electron-dense material, but also radiotransparent areas suggesting the negative image of a globular material (Fig. 5).

Discussion

Four cases of extensive, localized bone resorption in the femur following total hip replacement have been reported by Harris et al. [4]; in the same paper, these authors mention that they have knowledge of 11 other cases. Carlsson et al. [1] observed localized endosteal resorption in 33 total hip replacements from a series of 70 revisions carried out for aseptic loosening. Probably, this phenomenon is more common than is generally recognized. The report of this further case is prompted by a combination of factors:

1. A metal-on-metal prosthesis allows the exclusion of polyethylene as an agent stimulating a macrophagic reaction.
2. The sequence of events in this case shows a very rapid resorption of the bone after a period of 10 years, in the course of which no adverse reaction was observed.

Extensive, localized lysis of the bone is commonly observed in the presence of infection, but this seems unlikely in this patient, who had normal ESR and white cell count, negative cultures, and no inflammatory reaction in the histological sections.

A macrophagic reaction is the common response to the release of different classes of particulate materials from implants [2, 5, 6, 8, 9] and the cause of bone resorption when granulation tissue accumulates in the space between the implant and the bone [10, 11]. Release rate, number, and size of the particles are critical factors controlling the intensity of the macrophagic reaction [7]. Polyethylene particles have no role in this case, and the same holds true for metallic particles, since no opaque structures were observed in the cytoplasm of macrophages and X-ray energy-dispersive analysis was negative. Direct, histologic demonstration of radiotransparent cement is not possible because small fragments are dissolved in processing the specimens. However, the granular aspect of the macrophage cytoplasm and the radiotransparent material in lysosomes are consistent with the hypothesis that the material stimulating the macrophagic reaction was methylmethacrylate. It is further supported by the operative findings of cement fragmentation in the cases of Harris et al. [4] and in the one reported here. In contrast to what Carlsson et al. [1] observed, the tip of the stem was completely enveloped by the cement and the osteolysis extended symmetrically on both the inner and the outer cortex; therefore, no direct metal-bone contact may be advocated as the cause of bone resorption.

The particles may have a wide range in size: in the case studied they were small and had the appearence of a powder. To our knowledge, this has not been reported before and can explain the intense macrophagic reaction and the rapid, lytic evolution of the granuloma.

Self-curing acrylic cement may be considered a composite material, where granules of polymer are bonded together with recently polymerized monomer [3]; fragmentation of the cement may release the interlocking polymer in the form of a powder, as well as granules, which are observed in the tissues as spheres or large shreds in the wider size range (more than 100 μm).
Radiographic records in this case allow us to date the phenomenon of fragmentation to 10 years after implantation; its cause remains obscure, but at least two hypotheses can be suggested:

1. Aging, with changes in the physicochemical properties of the resin;
2. mechanical factors.

The observation of fragmentation in a limited area of the cement coating favors the latter or a combination of both.

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